

Social Dysfunction and Apathy: Transdiagnostic Domains in Late-Life Cognitive Disorders

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Abstract. Social dysfunction is a maladaptive process of coping, problem solving, and achieving one's goals. A new definition of apathy was cross-linked to social dysfunction, with a reduced goal-directed behavior and social interaction as a separate dimension. We hypothesized that these two neuropsychiatric symptoms may be included in the mild behavioral impairment diagnostic framework, operationalizing and standardizing late-life neuropsychiatric symptom assessment, to improve risk determination of dementia. Social dysfunction and apathy were transdiagnostic and prodromic for late-life cognitive disorders. A transdiagnostic approach could provide a useful mean for a better understanding of apathy and related conditions such as social behavior.

Keywords: Alzheimer's disease, apathy, biopsychosocial frailty, dementia, depression, late-life cognitive disorders, mild behavioral impairment, mild cognitive impairment, social dysfunction, social withdrawal

INTRODUCTION

Among late-life neuropsychiatric symptoms (NPS), social dysfunction and apathy are two macroscopic dimensions included in different neuropsychiatric conditions in older age. They not only

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assumed a transdiagnostic characteristic, but also a prodromic significance. Current knowledge fails to define the pathophysiological mechanisms that link system-level phenomena to the multiple hierarchies of brain function underlying social behavior and living. Social deficits such as social dysfunction and withdrawal can sometimes represent the first signs of several neuropsychiatric disorders, manifesting far before the full onset of the other symptoms.¹

Among recent diagnostic clinical criteria and definitions for apathy,^{2–4} the 2018 international consensus group about apathy pointed to the importance of adopting a transdiagnostic approach, which cuts across traditional disease boundaries, to provide useful means for better understanding of apathy and related conditions.³ In fact, the 2009 the European Psychiatric Association (EPA) diagnostic criteria suggested that apathy may be diagnosed based on a loss of or diminished motivation and the presence of at least one symptom in at least two of three domains of apathy (reduced goal-directed behavior, goal-directed cognitive activity, or emotions).² In the 2018 definition of apathy, the term motivation was replaced by goal-directed behavior, domains “were re-labelled “dimensions”; and a new separate dimension, social interaction, was introduced.³ Finally, behavioral and cognitive domains of apathy were subsumed under one category: in the clinical practice, it is difficult to dissociate cognitive from behavioral deficits, because both result in diminished observable activity.³

From a microscopic point of view, deficits in social cognitive processes have been identified as core cognitive deficits in neuropsychiatric disorders and have been reported to be among the strongest predictors of impaired social functioning in this populations and in different age strata.⁵ Social functioning is defined as an individual’s ability to perform appropriately everyday social tasks and consequently to maintain an adequate social life.⁶ Social dysfunction depends on individual inability in coping with stressful situational factors and achieving adequate social gratification and own goals. It could be defined as the maladaptive way to manage personal, interpersonal, or geographic environment.⁶ Based on the emergence of persistent NPS among non-demented individuals in later life, mild behavioral impairment (MBI) was associated with cognitive impairment and was suggested as an at-risk state for incident cognitive decline and dementia.^{7–9} These NPS included apathy, affective dysregulation, impulse dyscontrol, abnormal perception and thought content, and social

dysfunction. In the present article, we hypothesized the importance of the inclusion of apathy and social dysfunction in MBI and its adequate assessment for predicting cognitive disorders and dementia in later life.

APATHY AND SOCIAL DYSFUNCTION, MILD COGNITIVE IMPAIRMENT, AND ALZHEIMER’S DISEASE

Individual social roles were strongly dependent on age and may be affected by the presence of psychopathology.¹⁰ The dimension of social dysfunction was key in study of health and diseases in aging populations, especially cognitive decline.^{11,12} Most studies focused on only one measure of social dysfunction in older age, without proper validation and distinction across different dimensions including subjectivity, structural, and functional aspects. The Social Dysfunction Rating Scale (SDRS) addresses these requirements because it objectively quantifies dysfunctional interaction with the environment.¹³

SDRS was recently validated in older subjects. This scale could be a valid instrument to capture both size and quality of social dysfunction, both in subjects with psychiatric disorders and in normal subjects. Education and global cognitive functions were inversely correlated to SDRS, while a direct association with global psychopathology, depression, and apathy was found.¹⁴ Measures of five factors were identified according to original factorial analysis: Factor 1 – Apathetic-Detachment, Factor 2 –Dissatisfaction, Factor 3 – Hostility, Factor 4– Health-Finance Concern, and Factor 5 – Manipulative- Dependency.¹⁴ Most items were included in the first factor. In this study, we also found an inverse correlation between SDRS and global cognitive scores (Mini Mental State Examination), the level of education, and the executive dysfunction (Frontal Assessment Battery) was also found.¹⁴ The relation of negative social interactions with late-life cognitive disorders has not been extensively investigated, but one study found more frequent negative social interaction to be related to an increased risk of developing mild cognitive impairment (MCI).¹⁵

On the contrary, among affective NPS (aNPS, depression, apathy, anxiety, and irritability), apathy was the most frequent and persistent symptom in all types of dementia, since from prodromic phases.¹⁶ In particular, apathy showed to increase the risk of dementia progression in individuals with MCI.¹⁷ In

Table 1

Principal longitudinal studies investigating the risk/percentage of conversion from mild cognitive impairment to Alzheimer's disease (AD) associated to the presence of apathy at baseline

Study	Follow-up time (y)	Sample Size	Age (y)	AD diagnostic criteria	Association or percentage of AD conversion in relation to apathy
Palmer et al., 2010 ¹⁸	3.3	131	70.8 ± 6.5	NINCDS-ADRDA	HR: 6.9, 95% CI: 2.3–20.6
Rosenberg et al., 2013 ¹⁹	1.2	1,821	75.3 ± 9.3	CDR	HR: 1.38, 95% CI: 1.2–1.56
Guercio et al., 2015 ²⁰	1.4	75	74.7 ± 8.0	CDR	HR: 1.19, 95% CI: 1.09–1.3
Ruthirakuhan et al., 2019 ²¹	1.9	4,932	73.2 ± 9.2	NINCDS-ADRDA	HR: 1.24, 95% CI: 1.05–1.46
Dietlin et al., 2019 ²²	1.5	96	78.7 ± 5.6	CDR	HR: 3.02, 95% CI: 2.17–4.20
Roberto et al., 2021 ²³	2.3	2,137	74.6 ± 8.2	NIA-AA	50.3%
Salem et al., 2023 ²⁴	8.2	1,092	67.0 ± 5.0	NINCDS-ADRDA	36.1%

NINCDS-ADRA, National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association; HR, hazard ratio; CI, confidence interval; CDR, Clinical Dementia Rating; NIA-AA, National Institute of Aging and Alzheimer's Association.

fact, in a recent systematic review with meta-analysis including 11 studies with 9504 individuals, there was a significant association between apathy and dementia conversion from MCI [hazard ratio (HR)=1.54; 95% confidence interval (CI)=1.29–1.84], while a subgroup analysis showed a significant association between apathy and progression to AD in MCI individuals (HR = 1.31; 95% CI = 1.15–1.49).¹⁷ In Table 1, we showed the principal longitudinal studies investigating the risk of conversion from MCI to AD associated to the presence of apathy at baseline.^{18–24}

Since from the early phases, dementia physiopathology seemed to progressively impair social brain at multiple sites, starting from the structures that sustained motivation and goal directed behavior to the mentalizing network. An inverse or a bidirectional association could be hypothesized in dementia since social withdrawal itself may decrease motivation through stimuli deprivation in a vicious circle.²⁵ Social function is a complex phenotype, which is influenced by a variety of socio-demographic features, as well as by basic domain deficits, in attention, working memory, and sensory processing.¹ The enormous amount of brain processes required to initiate and maintain social relationships likely reflects an intrinsic vulnerability to pathological insults, which may result in social withdrawal far before the full onset of the disorder. Social withdrawal is likely preceded by subtle cognitive dysfunctions, which are difficult to detect clinically and are specific for dementia subtypes and their course.²⁶

Although different types of dementia (i.e., behavioral variant frontotemporal dementia, bvFTD, and AD) experienced declines in cognitive and socioemotional functioning over time, the pattern of decline appeared to differ since from the beginning. bvFTD patients experienced rapid decline in general cog-

nition, emotion recognition and sarcasm detection, whereas AD patients tended to show progressive decline in general cognition and sarcasm detection only. Specific cognitive deficits, such as word finding difficulty and face/emotional recognition, reduced engagement in social leisure activities leading eventually to social withdrawal. A cognitive domain such as subjective word-finding difficulty was uniquely related to social activity measures, rather than depressive symptoms. On the other hand, social withdrawal itself seemed to determine difficulties in activities of daily living which required cognitive input.²⁷ Linguistic markers predict onset of AD and other subtypes of FTD (primary progressive aphasia).²⁸

Some studies also explored the lived experience of NPS among people with MCI to explain the unique manifestations of NPS in a preclinical cohort.^{29,30} Cognitive deterioration, together with the resultant impacts on various life domains, evoked a cluster of NPS that compromised the overall well-being in preclinical subjects.²⁹ Psychological, emotional, and behavioral symptoms were not solely attributable to neurobiological pathways but also to how individuals may interact with the real world. There was also a differential impact of mild memory change on the everyday lives of older adults with age-normal memory changes and in those with amnesic MCI, with consequences more substantial and generally more adverse for amnesic MCI individuals.³⁰

CONCLUSIONS

In conclusion, in the present article, examining the importance of the inclusion of apathy and social dysfunction in MBI and its adequate assessment, we wanted to hypothesize the importance of early detection and interventions in dysfunctional aspects

of social competence in older age for predicting late-life cognitive disorders and dementia. The presence of social withdrawal and other negative-type symptoms (such as apathy) have been associated with categories of MCI at higher risk of conversion into dementia.³¹ NPS, particularly aNPS, in cognitively healthy older adults may be prodromal symptoms of AD.³² This concept has been termed MBI as a parallel concept to MCI.⁷ Social functioning and SDRS might be included in a risk index and use this to stratify older persons for biomarker assessment for cognitive and psychiatric health. Other constructs similar to MBI have been proposed as predictors of different types of dementia and MCI,^{33,34} i.e., the biopsychosocial frailty phenotype, with its coexistent biological/physical and psychosocial dimensions, defining a biological aging status and including motivational, emotional, and socioeconomic domains. This complex and multidimensional frailty phenotype has been associated with all-cause dementia, MCI, non-amnesic MCI, AD, AD neuropathology, vascular dementia, and non-AD dementias,^{33,34} suggesting that this construct may capture important aspects of assessment and targeted intervention in late-life cognitive disorders.

AUTHOR CONTRIBUTIONS

Madia Lozupone (Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing) Vittorio Dibello (Conceptualization; Methodology; Project administration; Validation; Visualization; Writing – review & editing) Rodolfo Sardone (Funding acquisition; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Writing – review & editing) Mario Altamura (Conceptualization; Funding acquisition; Investigation; Writing – review & editing) Antonello Bellomo (Conceptualization; Data curation; Supervision; Validation; Visualization; Writing – review & editing) Antonio Daniele (Conceptualization; Funding acquisition; Investigation; Supervision; Validation; Visualization; Writing – original draft) Vincenzo Solfrizzi (Conceptualization; Data curation; Supervision; Validation; Visualization; Writing – review & editing) Emanuela Resta (Conceptualization; Data curation; Funding acquisition; Investigation; Supervision; Validation; Visualization; Writing – review & editing)

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DECLARATION OF INTEREST

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. Dr Lozupone and Dr Panza are Editorial Board Members of this journal but was not involved in the peer-review process of this article nor had access to any information regarding its peer-review.

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